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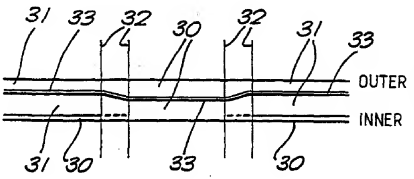

(57) Abstract

A composite continuously electrostatically spun synthetic vascular graft has a central graft portion having a first polymeric microfibrous structure (30) and end graft portions having a second microfibrous structure (31) including fibres of different diameter, transition between the first and second fibrous structure being sufficiently gradual to avoid sudden flexibility changes in the grafts between the central portions and the end portions. The graft is spun on a mandrel (10) by creating a central electrostatic field for creating the first fibrous structure and end fields surrounding end portions of the mandrel for creating the second fibrous structure, together with transitional fields between the centre and end fields to create the gradual change between the centre and end fields.

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IMPROVEMENTS IN SYNTHETIC VASCULAR GRAFTS AND THEIR METHODS OF MANUFACTURE

The invention relates to synthetic vascular grafts and methods of their manufacture.

Several publications of patent literature have taken place concerning production of synthetic vascular grafts by means of electrostatic spinning processes, for example UK-A-2121286, UK-A-2120946 and UK-A-2142870 and EP-A-223374A and EP-A-266035A. In general, a microfibrous structure is built up on a spinning, electrostatically charged mandrel. Spinning conditions can be varied (for example mandrel speed and the electrostatic field) to vary the fibrous structure of the graft.

Different fibrous structures have different advantages and disadvantages. For example, a microfibrous structure as described in UK-A-2121286 or UK-A-2120946 with filaments of a diameter of the order of 1μm to 2μm generally randomly oriented allows multiple needling without deterioration, but is somewhat stiff and difficult to bend to a desired configuration during surgery. Alternatively, a fibrous structure having a mixture of smaller diameter fibres (typically 1μm) and larger diameter fibres (typically 10μm) with voids in the structure, as described in EP-A-223374A, provides good flexibility without kinking, but does not have the same resistance to deterioration when exposed to multiple needling as does the structure described earlier.

According to the invention there is provided a composite, continuously electrostatically spun synthetic vascular graft comprising a central graft portion having a first polymeric microfibrous structure of fibres of substantially uniform diameter and end graft portions having a second microfibrous structure including fibres of different diameter, transition between the first and

second fibrous structures being sufficiently gradual to avoid sudden flexibility changes in the graft between the central portion and the end portions.

The second microfibrous structure preferably includes voids.

There may be an inner microfibrous layer of the first structure extending along the entire length of the graft.

A meld layer (that is a substantially impervious, non fibrous layer) may be present within the fibrous structure, and preferably extends along the length of the graft. The meld layer is preferably produced by electrostatic spinning of polymeric material under different electrostatic conditions.

The end portions, and possibly the entire graft, may be coated externally with an impervious layer of non-biodegradable material such as silicone rubber.

The invention further provides a method of producing a composite electrostatically spun synthetic vascular graft according to the invention comprising the steps of

1) rotating an electrostatically charged mandrel

2) directing fibreizable material at the mandrel

3) creating an electrostatic field surrounding the mandrel having a centre field surrounding a central mandrel portion for creating said first fibrous structure and end fields surrounding end portions of the mandrel for creating said second fibrous structure and

4) creating transitional fields between said centre field and said end fields such that there is gradual change between said centre and end fields.

The method may comprise an initial step of creating a field surrounding the mandrel to produce said first fibrous structure along the length of the graft, before altering the end fields to produce said second fibrous

structure.

The end and centre fields may be altered during graft production to create a substantially impervious melded layer along the length of the graft within the fibrous structure.

The method may include a further step of coating at least the end portions of a graft with impervious elastomeric material, for example silicone rubber.

The second fibrous structure is less dense than the first fibrous structure, and when the end portions have reached a desired thickness, the centre portion may be too thin. Accordingly, the method preferably provides a further step, when the end portions have reached a desired thickness, of altering the electrostatic field surrounding the mandrel to reduce deposition of fibres at the end portions but allow uninterrupted deposition of fibres at the centre portion.

The step of reducing deposition of fibres at the end portions is preferably achieved by charging conducting plates in the region of the end portions such that fibreizable material is attracted to the plates rather than the mandrel.

The invention further provides apparatus for electrostatically spinning a graft according to the invention, which apparatus comprises a mandrel, first electrostatically chargeable plate means to create an electrostatic field surrounding regions of the mandrel to collect the end portions of the graft, and second electrostatically chargeable plate means to create an electrostatic field surrounding a central portion of the mandrel.

The first plate means may comprise two pairs of parallel plates, the mandrel extending between the plates of each pair, and one pair lying at each end of the mandrel.

The second plate means may comprise a pair of parallel plates between which plates a central portion of the mandrel lies.

The plates of the second plate means may overlap the plates of the first plate means.

The plates of the second plate means may lie closer together than the plates of each pair of the first plate means.

The plates may be essentially rectangular, but preferably have rounded corners where the first plate means lie adjacent the second plate means.

By way of example, one embodiment of a graft, a manufacturing method, and apparatus according to the invention will now be described with reference to the accompanying drawings, in which:-

Figure 1 is a front elevation of apparatus according to the invention;

Figure 2 is a plan view of the apparatus of Figure 1;

Figure 3 is a table of voltages and flows;

Figure 4 is a view of an arm and an arterio-venous fistula graft; and

Figure 5 is an enlarged sectional view through a graft wall.

The apparatus of Figures 1 and 2 comprises a rotatable mandrel 10, the speed of rotation being variable but generally several hundred r.p.m. The mandrel 10 is electrostatically chargeable by known means. The mandrel is journalled in bearings 13 insulated from the remainder of the apparatus.

Above and below the mandrel 10 are arranged electrostatically chargeable plates, the plates being arranged in pairs to provide two pairs of end plates 11 and a pair of centre plates 12.

The centre plates 12 are closer together than the

end plates 11, and the plates 11 and 12 are arranged symmetrically about the mandrel 10 when viewed parallel to the plane of the plates, but the mandrel is located towards leading edges of the plates 11 and 12, as shown in the plan view of Figure 2.

The preferred form of apparatus shown in Figures 1 and 2 has end plates of length 320mm spaced 140mm apart, and centre plates 12 of length 112mm spaced 100mm apart. The end plates 11 overlap the centre plates 12 by 9mm each side. It will be appreciated that this embodiment may be subject to variation in dimensions and proportions.

A preferred sequence for using the apparatus of Figures 1 and 2 to produce a graft is as follows, reference being made to the table of Figure 3 in which kVA refers to the potential of the end plates 11, kVB refers to the potential of the centre plates 12, kVC refers to the potential of the mandrel, Q refers to the flow rate in ml per hour of fibreizable material in solution, and VOL refers to the volume of solution directed at the mandrel in each phase.

General reference is appropriate here to the UK and EP specifications referred to earlier, as general details of electrostatic spinning processes are provided therein, which details are assumed to be understood for the purposes of this specification. Publications referred to in the UK and EP specifications referred to earlier herein are similarly assumed to be understood.

The sequence of phases in fabricating a preferred embodiment of graft shown in Figure 4 is:-

Phase 1

The potentials in the table of Figure 3 lay down an inner layer of microfibres (diameter typically 1μm to 2μm) uniformly over the whole length of the mandrel. The potential of the centre plates 12 needs to be lower than

that of the end plates as the plates 12 are closer together. The microfibrous structure produced is similar to those described in UK-A-2121286 and UK-A-2120946, and other documents referred to therein.

Phase 2

Phase 1 is short lived. In Phase 2, the potential of the end plates 11 is increased, as is the flow rate of fibreizable material. This causes a more open fibrous structure to be formed on the mandrel in the regions of influence of the end plates 11, while the microfibrous structure of Phase 1 continues to build up in the central portion. The more open structure is substantially as described in EP-A-223374A.

Phase 3

The mandrel potential is greatly increased, and plate potentials are reduced, as is flow rate of fibreizable material. This causes a meld layer to be formed along the length of the graft since fibreizable material arrives at the mandrel before fibres are properly formed. Meld layer formation is described in EP-A-266035A.

Phase 4

The potentials and flow rates are returned to the conditions of Phase 2.

When Phase 4 is completed, a triple structure is formed, and the less dense outer portions have reached their desired thickness. The centre section, being compact, is too thin, so production is moved to Phase 5, where the end plates 11 are highly charged to attract almost all end region fibres directly to them instead of the mandrel. The centre plates 12 are maintained in the condition of Phases 1, 2 and 4 to allow uninterrupted deposition of microfibrous structure in the central region.

Transition between the centre section of the

graft and the end sections is achieved gradually, in this embodiment over a graft length of 2cm or so. Transition is achieved by overlap of the plates 11 and 12, and by rounding of the plate corners.

The method is conveniently computer controlled to provide continuous operation through the phases.

Figure 4 shows an arterio-venous fistula graft 20 according to the invention having a dense microfibrous structure 21 in a central portion, having good properties for multiple needling, and less dense end portions 22, 23 to provide flexibility needed during surgery. The flexible end portions 22, 23 may be silicone rubber coated (for example with SILASTIC - Trade Mark) or coated with other protective, flexible material.

Figure 5 shows a wall in diagrammatic section. Phase 1 microfibrous structure is shown at 30 (the first microfibrous structure) and the second microfibrous structure of the bulk of the end portions is shown at 31, transition portions being shown in the portions defined by lines 32. The meld layer is shown at 33.

It will be appreciated that modifications and alterations may be made to the apparatus, method and graft hereinbefore described, within the scope of the invention defined.

CLAIMS

1. A composite, continuously electrostatically spun synthetic vascular graft comprising a central graft portion having a first polymeric microfibrous structure (30) of fibres of substantially uniform diameter and end graft portions having a second microfibrous structure (31) including fibres of different diameter, transition between the first and second fibrous structures being sufficiently gradual to avoid sudden flexibility changes in the graft between the central portion and the end portions.

2. A graft as claimed in Claim 1 wherein the second microfibrous structure includes voids.

3. A graft as claimed in Claim 1 or Claim 2 comprising an inner microfibrous layer of the first structure (30) extending along the entire length of the graft.

4. A graft as claimed in any one of Claims 1 to 3 comprising a meld layer (33) within the fibrous structure (30, 31).

5. A graft as claimed in any one of Claims 1 to 4 wherein the meld layer extends along the length of the graft.

6. A graft as claimed in any one of Claims 1 to 5 wherein at least the end portions are coated with non-biodegradable material.

7. A method of producing a composite electrostatically spun synthetic vascular graft as claimed in any one of Claims 1 to 6 comprising the steps of:-

1) rotating an electrostatically charged mandrel (10)

2) directing fibreizable material at the mandrel (10)

3) creating an electrostatic field surrounding the mandrel (10) having a centre field surrounding a central mandrel portion for creating said first fibrous structure

(30) and end fields surrounding end portions of the mandrel (10) for creating said second fibrous structure (31) and

4) creating transitional fields between said centre field and said end fields such that there is gradual change between said centre and end fields.

8. A method as claimed in Claim 7 comprising an initial step of creating a field surrounding the mandrel (10) to produce said first fibrous structure (30) along the length of the graft, before altering the end fields to produce said second fibrous structure (31).

9. A method as claimed in Claim 7 or Claim 8 wherein the end and centre fields are altered during graft production to create a substantially impervious melded layer along the length of the graft within the fibrous structure.

10. A method as claimed in any one of Claims 7 to 9 including a further step of coating at least the end portions of a graft with impervious elastomeric material.

11. A method as claimed in any one of Claims 7 to 10 comprising, when the end portions have reached a desired thickness, of altering the electrostatic field surrounding the mandrel (10) to reduce deposition of fibres at the end portions but allow uninterrupted deposition of fibres at the centre portion.

12. A method as claimed in Claim 11 wherein the step of reducing deposition of fibres at the end portions is achieved by charging conducting plates in the region of the end portions such that fibreizable material is attracted to the plates rather than the mandrel.

13. Apparatus for electrostatically spinning a graft as claimed in any one of Claims 1 to 6, which apparatus comprises a mandrel (10), first electrostatically chargeable plate means (11) to create an electrostatic field surrounding regions of the mandrel (10) to collect the end portions of the graft, and second

electrostatically chargeable plate means (12) to create an electrostatic field surrounding a central portion of the mandrel (10).

14. Apparatus as claimed in Claim 13 wherein the first plate means comprise two pairs of parallel plates, the mandrel extending between the plates of each pair and one pair lying at each end of the mandrel.

15. Apparatus as claimed in Claim 13 or Claim 14 wherein the second plate means (12) comprise a pair of parallel plates between which plates a central portion of the mandrel lies.

16. Apparatus as claimed in Claim 15 wherein the plates of the second plate means overlap the plates of the first plate means.

17. Apparatus as claimed in Claim 15 or Claim 16 wherein the plates of the second plate means lie closer together than the plates of each pair of the first plate means.

18. Apparatus as claimed in any one of Claims 13 to 17 wherein the plates have rounded corners where the first plate means lie adjacent the second plate means.

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FIG. 1

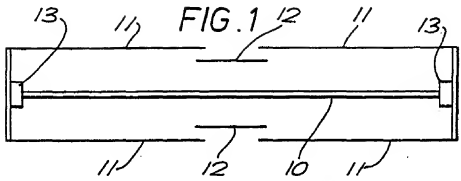


FIG. 2

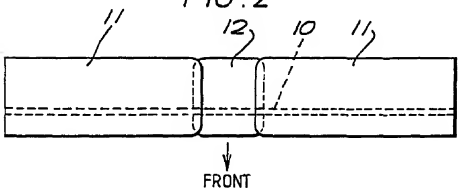


FIG. 3

PHASE	kV'A'	kV'B'	kV'C'	FLOW Q	VOL. ml.
1	8.0	6.5	9.0	1.2	— minute amount for 10 minutes only
2	11.2	6.5	9.0	7.5	30
3	8.5	4.0	17.0	3.0	3.0
4	11.2	6.5	9.0	7.5	10
5	13.2	6.5	9.0	7.5	15

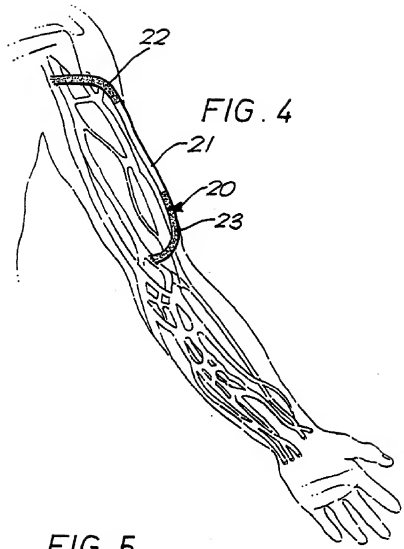
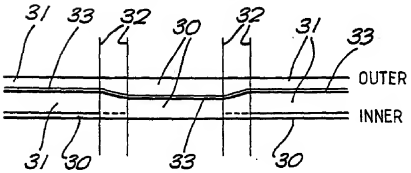


FIG. 4

FIG. 5



INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 90/01204

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)[5]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC5: A 61 F 2/06

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
IPC5	A 61 F

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category *	Citation of Document,[11] with Indication, where appropriate, of the relevant passages [12]	Relevant to Claim No.[13]
A	EP, A1, 0266035 (ETHICON INC.) 4 May 1988, see the whole document	1-18
A	GB, A, 2142870 (ETHICON INC) 30 January 1985, see the whole document	1-18

* Special categories of cited documents: [10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
22nd October 1990	22 11 90
International Searching Authority	**Signature of Authorized Officer**
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ANNEX TO THE INTERNATIONAL SEARCH REPORT
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The members are as contained in the European Patent Office EDP file on 27/09/90
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A1- 0266035	04/05/88	AU-D- 7775587	10/03/88
		GB-A- 2195251	07/04/88
		JP-A- 63119756	24/05/88
GB-A- 2142870	30/01/85	NONE	

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